

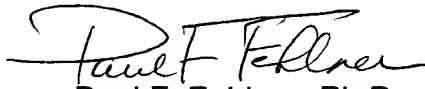
the specification and claims as filed. No new matter has been added. All pending claims are provided in an Appendix attached hereto.

Early and favorable action on this application is earnestly solicited.

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## APPENDIX

U.S. Patent Application Serial No. 08/930,480  
"Conditional Expression System"  
RPR File No. ST95021-US  
Claims Under Consideration

58. A bispecific chimeric molecule comprising a DNA bending domain capable of binding selectively to a defined DNA sequence and a regulatory domain capable of binding specifically to a transactivator, a transrepressor or a transactivating or transrepressing complex characteristic of a physiological or physiopathological state, wherein the chimeric molecule allows the selective recruitment of a transcriptional factor or complex whose activation or inactivation leads to a physiopathological situation, or any endogenous molecule or molecule of infectious origin whose presence or absence leads to a physiopathological situation.

59. The molecule according to claim 58, wherein the domain capable of binding selectively to a defined DNA sequence is derived from a eukaryotic protein.

60. The molecule according to claim 59, wherein the domain capable of binding selectively to a defined DNA sequence is derived from a protein selected from the group consisting of p53, a STAT protein, and an NFkB protein.

61. The molecule according to claim 58, wherein the domain capable of binding selectively to a defined DNA sequence is derived from a prokaryotic protein.

62. The molecule according to claim 61, wherein the prokaryotic protein is a bacterial repressor.

63. The molecule according to claim 61, wherein the domain capable of binding selectively to a defined DNA sequence is derived from a TetR protein.

64. The molecule according to claim 61, wherein the domain capable of binding selectively to a defined DNA sequence is derived from a Cro protein.

65. The molecule according to claim 58, wherein the domain capable of binding selectively to a defined DNA sequence consists of a full length protein.

66. The molecule according to claim 65, wherein the domain capable of binding selectively to a defined DNA sequence consists of a full length TetR protein.

67. The molecule according to claim 65, wherein the domain capable of binding selectively to a defined DNA sequence consists of a full length Cro protein.

68. The molecule according to claim 58, wherein the domain capable of binding specifically to the transactivator, the transrepressor or the transactivating or transrepressing complex is an oligomerizing domain.

69. The molecule according to claim 68, wherein the oligomerizing domain is selected from the group consisting of a leucine zipper, an SH3 domain, and an SH2 domain.

70. The molecule according to claim 68, wherein the oligomerizing domain capable of binding specifically to the transactivator consists of the C-terminal part of a p53 protein having an amino acid sequence as depicted in SEQ ID No. 3.

71. The molecule according to claim 58, wherein the domain capable of binding specifically to the transactivator, the transrepressor or the transactivating or transrepressing complex is a synthetic domain known to interact with the transactivator, the transrepressor or the transactivating or transrepressing complex.

72. The molecule according to claim 58, wherein the domain capable of binding specifically to the transactivator, the transrepressor or the transactivating or transrepressing complex is an antibody or an antibody fragment or derivative directed against the transactivator, the transrepressor or the transactivating or transrepressing complex.

73. The molecule according to claim 72, wherein the domain capable of binding specifically to the transactivator or the transactivating complex consists of a Fab or F(ab)'2 fragment of the antibody or a VH or VL region of the antibody.

74. The molecule according to claim 72, wherein the domain capable of binding specifically to the transactivator or the transactivating complex consists of a single-chain antibody (ScFv).

75. The molecule according to claim 58, wherein the DNA-binding domain and the transactivator-binding domain are linked to each other through an arm consisting of from 5 to 30 amino acids.

76. The molecule according to claim 75, wherein the arm consists of 5 to 20 amino acids.

77. The molecule according to claim 76, characterized in that the arm is chosen from a peptide sequence selected from the group consisting of SEQ ID No. 5 and SEQ ID No. 6.

78. The molecule according to claim 58, wherein the DNA-binding domain is situated at the N-terminal position and the transactivator-binding domain is situated at the C-terminal position.

79. The molecule according to claim 58, wherein the DNA-binding domain is situated at the C-terminal position and the transactivator-binding domain is situated at the N-terminal position.

80. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a transactivator-binding domain consisting of a single chain antibody (ScFv), a tag peptide sequence comprising SEQ ID Nos. 7 or 8, a peptide arm sequence comprising SEQ ID Nos. 5 or 6, and a DNA-binding domain consisting of a TetR or Cro protein.

81. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a transactivator-binding domain consisting of a single chain antibody (ScFv), a peptide arm sequence comprising SEQ ID Nos. 5 or 6 and a DNA-binding domain consisting of a TetR or Cro protein.

82. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a transactivator-binding domain consisting of a single chain antibody (ScFv), and a DNA-binding domain consisting of a TetR or Cro protein.

83. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a DNA-binding domain consisting of a TetR or Cro protein and a transactivator-binding domain consisting of a single chain antibody (ScFv).

84. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a DNA-binding domain consisting of a TetR or Cro protein, a peptide arm sequence comprising SEQ ID Nos. 5 or 6 and a transactivator-binding domain consisting of a single chain antibody (ScFv).

85. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a domain for oligomerization comprising SEQ ID No. 3, a tag sequence comprising SEQ ID Nos. 7 or 8, a peptide arm sequence comprising SEQ ID Nos. 5 or 6, and a DNA-binding domain consisting of a TetR or Cro protein.

86. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a

domain for oligomerization comprising SEQ ID No. 3, a peptide arm sequence comprising SEQ ID Nos. 5 or 6 and a DNA-binding domain consisting of a TetR or Cro protein.

87. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a domain for oligomerization comprising SEQ ID No. 3 and a DNA-binding domain consisting of a TetR or Cro protein.

88. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a DNA-binding domain consisting of a TetR or Cro protein and a domain for oligomerization comprising SEQ ID No. 3.

89. The molecule according to claim 58, wherein the molecule comprises in order from the N-terminal position to the C-terminal position: a DNA-binding domain consisting of a TetR or Cro protein, a peptide arm sequence comprising SEQ ID Nos. 5 or 6, and a domain for oligomerization comprising SEQ ID No. 3.

90. An isolated nucleic acid encoding a chimeric molecule according to claim 58.

91. The nucleic acid according to claim 90, wherein the nucleic acid is DNA.

92. A conditional system for the expression of a gene comprising:  
(a) the bispecific chimeric molecule as defined in claim 58, and  
(b) an expression cassette comprising a regulatory sequence, a minimal transcriptional promoter and a gene, wherein the bispecific chimeric molecule binds to the regulatory sequence whereby transcription activation occurs.

93. The conditional system according to claim 92, wherein the DNA-binding domain of the chimeric molecule is represented by all or part of TetR protein and a regulatory sequence comprises the sequence as depicted in SEQ ID No. 1.

94. The conditional system according to claim 92, wherein the DNA-binding domain of the chimeric molecule is represented by all or part of Cro protein and the regulatory sequence comprises a sequence as depicted in SEQ ID No. 2.

95. The conditional system according to claim 92, wherein the minimal promoter comprises an INR or a TATA box.

96. The conditional system according to claim 92, wherein the minimal promoter is derived from the promoter of a thymidine kinase gene.

97. The conditional system according to claim 92, wherein the minimal promoter is derived from the promoter of human CMV.

98. A vector comprising:

(a) a nucleic acid sequence encoding the bispecific chimeric molecule according to claim 58, and

(b) an expression cassette comprising a regulatory sequence, a minimal transcriptional promoter and a coding sequence of interest, wherein the bispecific chimeric molecule binds to the regulatory sequence whereby transcription activation occurs.

99. The vector according to claim 98, wherein a DNA-binding domain of the chimeric molecule is represented by all or part of TetR protein and the regulatory sequence comprises a sequence as depicted in SEQ ID No. 1.

100. The vector according to claim 98, wherein the DNA-binding domain of the chimeric molecule is represented by all or part of Cro protein and the regulatory sequence comprises a sequence as depicted in SEQ ID No. 2.

101. The vector according to claim 98, wherein the coding sequence of interest encodes a therapeutic product.

102. The vector according to claim 101, wherein the therapeutic product is toxic to a cell in which it is expressed.

103. A pharmaceutical composition comprising the vector according to claim 98 and a pharmaceutically acceptable vehicle.

104. An isolated nucleic acid comprising a sequence as depicted in SEQ ID No. 4.

105. The molecule according to claim 58, wherein the transactivator characteristic of a physiological or physiopathological state is a protein having a transcriptional transactivating activity.

106. The molecule according to claim 105, wherein the transactivator is a cellular protein.

107. The molecule according to claim 106, wherein the cellular protein is a p53 protein.

108. The molecule according to claim 58, wherein the transactivator or transactivating complex characteristic of a physiological or physiopathological state is a protein appearing in an infected or hyperproliferative cell.